CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA

FENBUTATIN OXIDE

Chemical Code # 1876, Tolerance # 362
SB 950 # 172

12/16/94, 1/12/02

I. DATA GAP STATUS

Chronic toxicity, rat:	No data gap, no adverse effect
Chronic toxicity, dog:	Data gap, inadequate study, no adverse effect indicated
Oncogenicity, rat:	No data gap, no adverse effect
Oncogenicity, mouse:	Data gap, inadequate study, no adverse effect indicated
Reproduction, rat:	No data gap, possible adverse effect
Teratology, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, no adverse effect
Neurotoxicity:	Not required at this time.

Toxicology one-liners are attached.

All record numbers through 146028 and 989032 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
File name: T020112
S. Morris, 1/12/02

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

CHRONIC TOXICITY, RAT

**362-006; 989020; "Toxicity Studies on the Pesticide SD 14114: Two Year Oral Experiment in Rats"; B.J. Simpson, G. Granville, and S.M. Doak; Tunstall Laboratory; Report # TLGR.0034.73; November 1973. Groups of 144 (control) or 72 (treated) Carworth Farm E rats per sex were fed dietary mixtures for 2 years of fenbutatin oxide [SD 14114, Hexakis (b,b-dimethylphenethyl) distannoxane, 97% (w/w) stated purity] at 0 (control), 50, 100, 300, or 600 ppm. Interim sacrifices were at 3 months (12/sex/control group and 6/sex/treated group), 6 months (24/sex/control group and 12/sex/treated group), and 12 months (12/sex/control group and 6/sex/treated group). Slower growth in the first weeks and lower body weight through most of the study were reported at 300 ppm in females and 600 ppm in both sexes. Serum alkaline phosphatase was increased in females at 100 ppm and both sexes at 300 and 600 ppm. Testes weights were increased in males at 600 ppm. Absolute and relative kidney weights were reduced in males at 50, 100, and 300 ppm and both sexes at 600 ppm. NOEL = 100 ppm (body weight). No adverse effect was indicated. The study was unacceptable(C. Aldous, 8/9/85) but upgraded by submission of adequate analysis of the test material, a summary of pathology data, list of tissues analyzed, survival data, food consumption, pathology and histopathology data and rationale for the doses used (S. Morris and J. Gee 1/12/02).

362-005; 024174: This document contains a brief summary of DPR doc. # 362-006, rec. # 989020. No worksheet was done (S. Morris, 10/22/93).

362-009; 018351: This document contains a brief summary of DPR doc. # 362-006, rec. # 989020. No worksheet was done (S. Morris, 10/22/93).

362-030; 036572: This document contains a retabulation of tumor incidence from the study at DPR doc. # 362-006, rec. # 989020. Evaluation of these data did not result in a change in study status. No worksheet was done (S. Morris, 10/27/93).

362-030; 036573: This document contains an exact duplicate of DPR doc. # 362-006, rec. # 989020. No worksheet was done (S. Morris, 10/27/93).

362-055; 116008: This document contains analysis of batch no. 6-2-0-0 of the test material used in the study at DPR doc. # 362-006, rec. # 989020. Evaluation of these data did not result in a change in study status. No worksheet was done (S. Morris, 10/22/93).

362-067; 143489: This document contains analysis of the test material, survival, pathology and histopathology data and a rationale for the doses used in the study at DPR doc. # 362-006, rec. # 989020. Evaluation of these data upgraded the study to acceptable. See Response, 1/12/02(S. Morris and J. Gee, 1/12/02).

362-070; 144767: This document contains samples of raw pathology and histopathology data sheets for the study at DPR doc. # 362-006, rec. # 989020. Evaluation of these data upgraded the study to acceptable. See Response, 1/12/02(S. Morris and J. Gee, 1/12/02).

362-071; 146029: This document summary pathology data sheets for the study at DPR doc. # 362-006, rec. # 989020. Evaluation of these data upgraded the study to acceptable. See Response, 1/12/02(S. Morris and J. Gee, 1/12/02).

CHRONIC TOXICITY, DOG

362-006; 989021; "Toxicity Studies on the Pesticide SD 14114: Two Year Oral Toxicity Test in Dogs"; G.C. Granville and K.M. Dix; Sittingbourne Laboratories, Sittingbourne, Kent, England; Report # TLGR.0035.73; November 1973. Groups of 8 (control) or 4 (treated) beagle dogs per sex were given fenbutatin oxide [SD 14114, hexakis(b,b-dimethylphenethyl)distannoxane, technical material, 97% stated purity] orally in gelatin capsules for 2 years at 0, 2.5, 5.0, 15.0, 30.0, or 60.0 mg/kg/day. No adverse effects were indicated. Body weight gain was decreased in both sexes at 60 mg/kg/day. Vomiting was seen at all doses and persisted in the 15, 30 and 60 mg/kg/day groups. NOEL = 5 mg/kg/day (vomiting incidence, body weight). The study was unacceptable and not upgradeable because there were no data on ophthalmology and food consumption(J. Schreider, 7/3/85; J. Gee and S. Morris 1/12/02).

362-005; 024175: This document contains a summary of the study at DPR doc. # 362-006, rec. # 989021. No worksheet was done (S. Morris, 10/22/93).

362-009; 018352: This document contains a summary of the study at DPR doc. # 362-006, rec. # 989021. No worksheet was done (S. Morris, 10/22/93).

362-052; 115004: This document contains body weight, organ weight, urinalysis, clinical chemistry, hematology, gross pathology, and histopathology data for the study at DPR doc. # 362-006, rec. # 989021. Evaluation of these data did not result in a change in study status. No worksheet was done (S. Morris, 10/22/93).

362-055; 116008: This document contains analysis of batch no. 6-2-0-0 of the test material used in the study at DPR doc. # 362-006, rec. # 989021. Evaluation of these data did not result in a change in study status. No worksheet was done (S. Morris, 10/22/93).

362-066; 143488: This document contains estimated food consumption and clinical observations for the study at DPR doc. # 362-006, rec. # 989021. The clinical data are adequate. Evaluation of these data changed the study status to not upgradeable. See DPR Response, 1/12/02, S. Morris and J. Gee).

362-071; 146028: This document contains samples of raw pathology data for the study at DPR doc. # 362-006, rec. # 989021. These data are adequate. Evaluation of these data did not result in a change in study status. No worksheet was done (See DPR Response, 1/12/02, S. Morris and J. Gee).

ONCOGENICITY, RAT

See under chronic rat.

ONCOGENICITY, MOUSE

362-030; 036574; "Toxicity Studies on the Pesticide SD14114: An 18 Month Feeding Study in Mice", TLGR.0036.73; G.C. Granville, B.J. Simpson, and S.M. Doak; Tunstall Laboratory, Sittingbourne, Kent, England; 11/73. Fenbutatin oxide [SD 14114, hexakis (b,b-dimethylphenethyl) distannoxane, 97% (w/w) stated purity, batch ref. FC 5894] was fed in the diets of groups of 120 (control) or 60 (treated) mice/sex at 0, 50, 100, 300, or 600 ppm. At 6 and 12 months, 12 control or 6 treated mice/sex/group were sacrificed. The surviving mice were sacrificed at 18 months. There was a treatment-related effect on body weight at 300 and 600 ppm (NOEL = 100 ppm). There were no treatment-related effects on survival, clinical signs or pathological, hematological, clinical chemical or histopathological findings. No adverse effect was indicated. The study is unacceptable and not upgradeable because adequate analytical, differential blood count, and food consumption data and a complete study protocol are not available (H. Green and S. Morris, 12/16/94; J. Gee and S. Morris, 1/12/02).

362-005; 024173: This document contains a brief summary of DPR doc. # 362-030, rec. # 036574. No worksheet was done (S. Morris, 10/22/93).

362-009; 018350: This document contains a brief summary of DPR doc. # 362-030, rec. # 036574. The document was not evaluated because of insufficient information for assessment (J. Schreider, 7/2/85).

362-051; 115003: This document contains pathology and histopathology tables for the study at DPR doc. # 362-030, rec. # 036574. Evaluation of these data did not result in a change in study status. No worksheet was done (S. Morris, 10/22/93).

362-055; 116008: This document contains analysis of batch no. 6-2-0-0 of the test material used in the study at DPR doc. # 362-030, rec. # 036574. Evaluation of these data did not result in a change in study status. No worksheet was done (S. Morris, 10/22/93).

362-068; 143490: This document contains a one-page study protocol, analysis of the diet used on a different study, limited hematology data and estimated injestion of test material for the study at DPR doc. # 362-030, rec. # 036574. Evaluation of these data changed the study status to not upgradeable (See DPR Response 2/12/02, J. Gee and S. Morris).

REPRODUCTION, RAT

362-006; 989025; "Results of Reproduction Study of Rats Fed Diets Containing SD14114-U Over Three Generations"; C.H. Hine; The Hine Laboratories, Inc., San Francisco, CA; Report # 33; October 1973. Groups of 20 female or 10 male Long-Evans rats were fed dietary mixtures of fenbutatin oxide (SD14114-U, 98% stated purity) at 0, 50, 100, or 300 ppm beginning 63 days prior to mating through 3 generations with 2 litters per generation. Decreased parental body weight, pup body weight, and pup survival (F3) were seen at 300 ppm. Reduced parental testes/body weight ratios were seen in males at 100 and 300 ppm. Decreased F1b pups per litter were seen at 300 ppm. No adverse effect was indicated. The study was unacceptable and not upgradeable because of insufficient numbers of animals, insufficient clinical observations, incomplete necropsy/histopathology, lack of pup and litter data, and inadequate dosing rationale (J. Schreider, 7/11/85).

362-005; 024176: This document contains a brief summary of DPR doc. # 362-006, rec. # 989025. No worksheet was done (S. Morris, 10/25/93).

362-009; 018354: This document contains a brief summary of DPR doc. # 362-006, rec. # 989025. No worksheet was done (S. Morris, 10/25/93).

362-030; 036576: This document contains a duplicate of DPR doc. # 362-006, rec. # 989025. No worksheet was done (S. Morris, 10/25/93).

**** 362-053; 115005;** "Reproductive and Fertility Effects with Vendex* Technical (IN Y4332-5) Multigeneration Reproduction Study in Rats", HLR 128-90; K.S. Bentley; Haskell Laboratory, Newark, DE; 6/15/90. Fenbutatin oxide (Vendex* technical, 99% purity) was continuously fed in the diets of 30 Crl:CD*BR rats/sex/group at 0, 40, 75, 250, or 500 ppm for 2 generations (F0, F1) with 1 litter per generation (F1, F2). The adult F0 rats were exposed for 72 days then mated. The F1 generation was exposed in utero and via lactation. At weaning, 30 pups/sex/group were continuously exposed to their respective diets for at least 105 days. The F1 adults were then mated and exposures were continued until terminal sacrifice of the F2 pups at weaning. A treatment-related decrease in mean body weight gain was seen at 500 ppm in F0 and F1 parental males and females (NOEL = 250 ppm). A **possible adverse effect** was indicated by decreased pup weight gain in F1 and F2 males and females at 500 ppm (NOEL = 250 ppm). The study was acceptable (H. Green and S. Morris, 12/16/94).

TERATOLOGY, RAT

362-030; 036581; "Teratology Study in Rats Given SD 14114 by Gavage", Report # TLGR.80.145; K.M. Dix; Sittingbourne Research Centre, Sittingbourne, Kent, England, 3/80. Fenbutatin oxide [SD 14114, hexakis(2-methyl-2-phenylpropyl)-distannoxane, batch # 7-13-0-0, 98.7% stated purity] was given by oral gavage (suspended in 0.5% carboxymethyl cellulose, 1.0% Pluronic F127) to 27 mated female Wistar rats per group at 0, 15, 30, or 60 mg/kg/day on gestation days 6 through 15. Maternal effects were increased incidences of diarrhea at 60 mg/kg/day and lower group mean body weights at 30 and 60 mg/kg/day (maternal NOEL = 15 mg/kg/day). There were no developmental effects reported (developmental NOEL = 60 mg/kg/day). No adverse effect was indicated. The study is unacceptable and not upgradeable because an adequate rationale for the doses used and analysis of the dosing solutions are not available(J. Schreider, 6/4/85; H. Green and S. Morris, 11/16/94; J. Gee and S. Morris, 1/12/02).

362-002; 989024: "Teratology Study in Rats Given SD 14114 (Vendex® Mitocide) by Gavage. Summary of TLGR.80.145"; K.M. Dix; Tunstall Laboratory; March, 1980. This document contained a summary of the study at DPR doc. # 362-030, rec. # 036581. This report was found unacceptable due to insufficient information (J. Schreider, 6/4/85).

362-065; 143487: This document contains analytical data for the test material for the study at DPR doc. # 362-065, rec. # 143487. Evaluation of the data changed

the study status to not upgradeable (See DPR Response, 1/12/02, S. Morris and J. Gee).

TERATOLOGY, RABBIT

** 362-030; 036580; "Teratology Study in New Zealand White Rabbits Given SD 14114", Report # SBGR.81.055; K.M. Dix; Sittingbourne Research Centre, Sittingbourne, Kent, England; May 21, 1981. Fenbutatin oxide [Vendex, SD 14114, hexakis(2-methyl-2-phenylpropyl)-distannoxane, batch # 7-13-0-0, 98.7% stated purity] was given orally in gelatin capsules to 18 or 23 mated New Zealand White female rabbits per group at 0 (empty capsule), 1, 5, or 10 mg/kg/day on gestation days 6 through 18. Maternal treatment-related effects at 5 and 10 mg/kg/day were death, gastric lesions, decreased food consumption, decreased fecal pellet production, and decreased group mean body weights relative to controls (maternal NOEL = 1 mg/kg/day). Developmental treatment-related effects were abortions and total resorptions at 5 and 10 mg/kg/day and reduced mean fetal weight at 10 mg/kg/day (developmental NOEL = 1 mg/kg/day). No treatment-related increases in fetal malformations or retardations were reported. No adverse effect was indicated (maternal NOEL = developmental NOEL). The unacceptable study (J. Schreider, 6/4/85) was upgraded by submission of a complete report (H. Green and S. Morris, 11/4/93).

362-002; 989023, "Teratology Study in New Zealand White Rabbits Given SD 14114 (Vendex* Mitocide) Orally. Summary of SBGR.81.055"; K.M. Dix; Tunstall Laboratory; 5/21/81. This summary of the study at DPR doc. # 362-030, rec. # 036580 was found unacceptable due to insufficient information (J. Schreider, 6/4/85).

362-030; 036579; "Toxicity Studies with SD 14114: Teratological Studies in Rabbits Given SD 14114 Orally", Report # TLGR.0052.72; K.M. Dix and A.B. Wilson; Tunstall Laboratory, Sittingbourne, Kent, England; January 1973. Fenbutatin oxide [SD 14114, hexakis(b,b-dimethylphenethyl)distannoxane, batch # 6-2-0-0, 97% w/w stated purity] was given orally in gelatin capsules to groups mated female albino Dutch rabbits at 0 (empty capsule), 3, or 10 mg/kg/day on gestation days 6 through 18. In experiment A there were 26 (control) or 15 (treated) animals / group and in experiment B there were 30 (control) or 20 (treated) animals / group. The "A" animals were killed on gestation day 28 and the "B" animals were killed on gestation day 29. There were no treatment-related maternal or developmental effects. There were no treatment-related increases in fetal malformations or retardations. No adverse effect was indicated (maternal NOEL = developmental NOEL = 10 mg/kg/day). The study was unacceptable and not upgradeable because there were insufficient analytical data, only two dose levels, inadequate rationale for the doses used, insufficient information about the age of the animals and animal care, and all fetuses were not examined viscerally and skeletally (H. Green and S. Morris, 12/16/94).

GENE MUTATION

** 362-045; 069879; "Mutagenicity Evaluation of Vendex® Technical in the CHO/HPRT Assay", HLR 128-88; R.G. Stahl; Haskell Laboratory, Newark, DE; 3/30/88. Fenbutatin oxide [distannoxane, hexakis(2-methyl-2-phenylpropyl)-; 99.4% stated purity; acetone vehicle] was evaluated for mutagenic potential by measuring the rate of mutation at the hypoxanthine-guanine phosphoribosyl transferase (HPRT) locus. Duplicate cultures of Chinese Hamster ovary (CHO) cells were exposed with metabolic activation (9000 x g supernatant of Aroclor® 1254-induced, male, Crl:CD®BR rat liver homogenate) to 0, 0.05, 0.5, 1.0, 2.5, 5.0, or 7.5 µg/ml for 5 hours or without activation to 0, 0.025, 0.05, 0.25, 0.5, 1.0, or 1.5 µg/ml for 18 to 19 hours. Each culture was subcultured 3 times in 7 days then plated at 2×10^5 cells / dish (5 dishes / treatment) and grown up in the presence of 1×10^{-5} 6-thioguanine (6-TG) for 6 to 8 days. Mutation frequency was determined by staining and counting 6-TG-resistant colonies. There were two trials. There was no treatment-related increase in mutation frequency. No adverse effect was indicated. The study was acceptable (H. Green and S. Morris, 12/16/94).

362-044; 069878; "Mutagenicity Testing of Vendex® Technical in the Salmonella typhimurium Plate Incorporation Assay", HLR 740-87; G.T. Arce; Haskell Laboratory, Newark, DE; 12/22/87. Fenbutatin oxide [Vendex* technical; distannoxane, hexakis(2-methyl-2-phenylpropyl); 98% stated purity; acetone vehicle] was tested in a reverse mutation assay on histidine auxotrophic strains of Salmonella typhimurium (TA97, TA98, TA100, and TA1535). Duplicate plates were exposed to 0, 5, 10, 50, 100, or 300 µg/plate/strain for 48 hours with or without S-9 metabolic activation (9,000 x g supernatant of Aroclor 1254-induced, male, Crl:CDBR rat liver homogenate). There was no treatment-related increase in reversion to prototrophy. No adverse effect was indicated. The study was unacceptable but possibly upgradeable with submission of adequate analytical data and rationale for the doses used (H. Green and S. Morris, 12/16/94).

362-054; 115006: This document contains a detailed protocol for the study at DPR doc. # 362-044, rec. # 069878. No worksheet was done (S. Morris, 12/1/93).

CHROMOSOME EFFECTS

** 362-045; 069880; "In Vitro Evaluation of Vendex® Technical (IN Y4332-5) for Chromosome Aberrations in Human Lymphocytes", HLR 69-88; D.A. Vlachos; Haskell Laboratory, Newark, DE; 3/2/88. Cultured human lymphocytes were exposed to fenbutatin oxide (Vendex® technical, 99.4% stated purity, acetone vehicle) for three hours in duplicate with or without metabolic activation (S-9 fraction of Aroclor® 1254-induced, male Crl:CD*BR rat liver homogenates) at 0 (untreated), 0 (vehicle), 0.7, 1.0, 2.5, 4.0, 5.0, or 7.0 µg/ml. The cultures were washed and incubated in medium for 24-26 hours with 0.1 ml/ml Colcemid® present for the last 2-2.5 hours. The cells were fixed and stained and 100 metaphase cells / treatment were microscopically examined for chromosome aberrations. Two trials were conducted. There was no treatment-related increase in chromosome aberrations. No adverse effect was indicated. The study was acceptable (H. Green and S. Morris, 12/16/94).

** 362-045; 069881, "Mouse Bone Marrow Micronucleus Assay of Vendex® Technical", HLR 71-88; D.A. Vlachos; Haskell Laboratory, Newark, DE; 3/14/88. Fenbutatin oxide [distannoxane, hexakis (2-methyl-2-phenylpropyl)-]; 99.4% stated purity was given to 5 or 6 Crl:CD*-1(ICR)BR mice/sex/group/time point by oral gavage (corn oil vehicle) at 0, 500, 2500, or 5000 mg/kg. Femur bone marrow samples were taken by serial sacrifice at 24 (all doses), 48 (0, 5000 mg/kg), or 72 hours (0, 5000 mg/kg) after dosing. Bone marrow smears were prepared, stained, and 1000 polychromatic erythrocytes were microscopically scored for micronuclei. There was no treatment related effect on the frequency of micronuclei. No adverse effect was indicated. The study was acceptable (H. Green and S. Morris, 12/16/94).

362-006; 989032; "Toxicity Studies with SD 14114: The Cytogenetic Investigation of Bone Marrow Cells of Mice After a Single Oral Dose of SD 14114"; B.J. Dean; Tunstall Laboratory; Report # TLGR.0042.72; October 1972.
Eight CF1 mice/sex/group were given suspensions of fenbutatin oxide [SD 14114, hexakis (b-b-dimethylphenylethyl)distannoxane, technical quality, 97% stated purity, 1% carboxymethyl cellulose vehicle] by oral gavage at 0, 500, or 1000 mg/kg. Ninety minutes before sacrifice, mitosis was arrested by intraperitoneal injections of Colcemid at 10 mg/kg. Eight or 24 hours after dosing the animals were sacrificed, femoral bone marrow was harvested, metaphase spreads of 100 cells / animal were examined for chromosome abnormalities. No adverse effect was indicated. The study was unacceptable and not upgradeable because there was no positive control, inadequate rationale for the doses, incomplete description of methods, not enough time points, and no individual data (J. Schreider, 7/2/85).

> 362-009; 018356: This document contains a brief summary of DPR doc. # 362-006, rec. # 989032. No worksheet was done (S. Morris, 10/25/93).

> 362-030; 036577: This document contains a duplicate of DPR doc. # 362-006, rec. # 989032. No worksheet was done (S. Morris, 10/25/93).

362-006; 989029; "Toxicity Studies with SD 14114: The Effect of a Single Oral Dose of SD 14114 on Dominant Lethal Mutations in Male Mice"; B.J. Dean and S.M. Doak; Tunstall Laboratory; Report # TLGR.0015.72; April 1972. Fenbutatin oxide [SD 14114, hexakis (b-b-dimethylphenylethyl)distannoxane, technical quality, 97% stated purity, 1% carboxymethyl cellulose vehicle] was give by oral gavage to 16 (control) or 8 (treated) male CF1 mice per group at 0, 250, or 500 mg/kg. Each male was caged with 3 new females per week for 8 weeks. Thirteen days after presumed mating, the females were killed and their uteri were examined for live fetuses and early and late fetal deaths. No adverse effect was indicated. The study was unacceptable and not upgradeable because of the lack of experimental details, no justification of the doses selected, only 2 treatment groups, no analytical data and no individual data or observations (J. Schreider, 6/4/85).

> 362-005; 024177: This document contains a brief summary of DPR doc. # 362-006, rec. # 989029. No worksheet was done (S. Morris, 10/25/93).

362-009; 018356: This document contains a brief summary of DPR doc. # 362-006, rec. # 989029. No worksheet was done (S. Morris, 10/25/93).

362-030; 036578: This document contains a duplicate of DPR doc. # 362-006, rec. # 989029. No worksheet was done (S. Morris, 10/25/93).

DNA DAMAGE

362-006; 989026; "Toxicity Studies with SD 14114: Genetic Studies with SD 14114 in Micro-Organisms in vitro and in the Host-Mediated Assay"; B.J. Dean, S.M.A. Doak, and J. Funnell; Tunstall Laboratory; Report # TLGR.0025.72; November 1972. Fenbutatin oxide [SD 14114, hexakis(b-b-dimethylphenylethyl) distannoxane, technical quality, 97% stated purity] was used in an in vitro mitotic gene conversion assay in which single suspensions of Saccharomyces cerevisiae D4 were exposed for 5 or 18 hours to 0.0, 0.0025, 0.005, or 20 µg/ml/time point. Each sample was seeded 8 times onto tryptophan- or adenine-free culture medium to isolate prototrophic colonies. The test material was also used in a host-mediated assay in which 2 male mice per group received 2 ml of S. cerevisiae culture by intraperitoneal injection followed by oral dosing with test material at 0 (1% carboxymethyl cellulose), 250, and 500 mg/kg. The cells were harvested 5 hours later and each sample was seeded 4 times onto tryptophan- or adenine-free culture medium to isolate prototrophic colonies. No adverse effects were indicated. The study was unacceptable and not upgradeable because of an inadequate protocol and dosing rationale and no individual data (J. Schreider, 5/2/85).

362-009; 018356: This document contains a brief summary of DPR doc. # 362-006, rec. # 989026. No worksheet was done (S. Morris, 10/25/93).

** 362-045; 069882; "Assessment of Vendex® Technical in the In Vitro Unscheduled DNA Synthesis Assay in Rat Primary Hepatocytes", HLR 130-88; K.S. Bentley; Haskell Laboratory, DE; May 3, 1988. Fenbutatin oxide [distannoxane, hexakis(2-methyl-2-phenylpropyl)-; 99.4% stated purity] was tested for unscheduled DNA synthesis (UDS) at concentrations of 0, 0.001, 0.005, 0.010, 0.050, 0.10, 0.50, 1.0, 5.0, 10.0, or 50.0 µg/ml 1% acetone. Samples of primary hepatocytes from male Crl:CD®BR rats were allowed to attach to 2 chamber slides / sample then exposed for 18 hours to the test solutions in the presence of 3H-thymidine. The cells were fixed, stained, and prepared for autoradiographic analysis. UDS was determined by estimating the number of silver grains of the nuclei of 25 cells / slide. Two trials were conducted. A treatment-related increase in UDS was not seen. No adverse effect was indicated. The study was acceptable (H. Green and S. Morris, 12/16/94).

362-054; 115007: This document contains an exact duplicate of DPR doc. # 362-045, rec. # 069882. No worksheet was done (S. Morris, 11/18/93).

NEUROTOXICITY

Not required at this time.

362-030; 036582; "Toxicology of the pesticide SD 14114: Comparative oedema assay of organotin compounds for oedema formation in the central nervous system of rats", Report TLGR.0026.72; G.M.R. Samuels and K.M. Dix; Sittingbourne Laboratories. The ability of fenbutatin-oxide to produce brain oedema in rats was assessed. No adverse effect was indicated. The study was not evaluated for acceptability and no worksheet was done (S. Morris, 12/17/93).

SUPPLEMENTAL INFORMATION

362-030; 036575; "Investigation of the Effects of a Single Oral Dose of SD14114 on the Reproductive Tract of the Male Rabbit", SBGR.81.258, K.M. Dix; Sittingbourne Research Centre; Sittingbourne, Kent, England; 1/7/82. Fenbutatin oxide (98.3% stated purity, carboxymethyl cellulose vehicle) was given by single oral gavage to groups of 12 (control) or 8 (treated) New Zealand White male rabbits at 0, 100, 500, or 1500 mg/kg. For each treated animal, there was a vehicle control animal, paired by weight, that received the same amount of food as the treated animal ate. Twenty-one days after dosing, the surviving rabbits were sacrificed and necropsied. The testes were weighed and gross and histopathological examinations of the reproductive tracts were performed. Lethalities in the 100, 500, and 1500 mg/kg groups were respectively 1/8, 1/8, and 5/8. Reduced food consumption and body weight were reported at 100, 500, and 1500 mg/kg. Mild gastric irritation was seen at 100 mg/kg. Severe irritation to the gastro-intestinal tract was reported at 500 and 1500 mg/kg. Hypoactivity and sloughing of the testicular germinal epithelium was attributed to malnutrition because they were seen in the treated and paired controls. No adverse effect was indicated. No worksheet was done (H. Green and S. Morris, 12/7/93).

362-005; 988987,
362-008; 988998,
362-009; 988998: These documents contain brief summaries of chronic toxicity studies in rat, mouse, and dog; a reproduction study in rat; and in vivo and in vitro gene mutation and chromosome aberration studies. No worksheets were done (S. Morris, 12/17/93).